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FIBRIN FOAM

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8 Claims. (Cl. 167—74)

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This invention relates to fibrin clots having a porous structure of low density and to methods for preparing the same. The fibrin clots may be conveniently referred to as fibrin foam.

A main object of the invention is the production of a hemostatic agent for use in elective surgery to control bleeding of all kinds, for instance from oozing surfaces such as cut bone surfaces, dura mater, muscle, or to control freely bleeding surfaces such as a lacerated venous sinus, torn veins, tumor beds, and the like. As a first aid hemostatic agent, the foams may be used primarily as dressing for lacerations.

A serious drawback of many widely used hemostatic techniques, for instance pressure application of sponges and pledgets saturated with saline solution, or thrombin or other clotting agents, lies in the fact that the materials used in such techniques must eventually be separated and removed from the oozing or bleeding surface. In so separating and removing the materials, the clot which has been formed is usually pulled away so that hemostasis is lost, and often the technique must be repeated. Fibrin foam of this invention, in contrast to usual hemostatic agents, has the marked advantage that it can be left permanently in a wound and therefore its use avoids the disturbances which necessarily accompany separation and removal. The foam is eventually absorbed by the human body.

While fibrin clots derived from blood plasma, including fibrin sheets, filaments, tubes, blocks and the like, are described in copending applications of John D. Ferry and Peter R. Morrison, the present invention provides a fibrin clot in the form of a foam, admirably suited for hemostatic purposes. Its low density porous absorbent structure permits the clot to absorb greater volumes of tissue fluids than a solid clot and to soak up greater volumes of blood. It can also soak up a large volume of a clotting agent such as thrombin solution, which is then available for hemostasis when applied to a bleeding area. Its flexible, doughy and resilient nature, when moistened, also permits it to be worked into suitable shaped pieces and to conform to irregular surfaces to which it is applied.

While the properties of fibrin foam of this invention may be varied as hereinafter described, according to the proportion of ingredients and the technique of preparation, a present preferred density for a dry foam is an average of 0.032 gram per cc.

Furthermore, in one form of the invention, the dry foam contains an excess of a clotting agent,

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such as purified thrombin, which is available for hemostasis.

Fibrin foams of this invention may be prepared from fractions of human blood plasma obtained in accordance with methods described in copending applications of Edwin J. Cohn. Purified fibrinogen fractions of the plasma may be converted into fibrinogen solutions of desirable properties for use in the preparation of fibrin foams, by methods set forth in the previously mentioned Ferry et al. applications.

As an example of such preparation of a suitable fibrinogen solution, the following is given:

The corpuscles are first removed from the blood by centrifugation, clotting of the fibrinogen being prevented by the addition of citrates or like agents. The plasma remaining after the separation of the corpuscles may then be treated for the precipitation therefrom of fibrinogen by cooling the same to 0° C. to —3° C. and adding thereto an organic precipitant, for example an alcohol such as ethanol. Ethanol may be added in amounts sufficient to constitute 8 to 10 per cent by volume of the plasma. The hydrogen ion concentration and the ionic strength of the plasma are also preferably adjusted. The pH of the solution may be controlled by the addition of acids or alkalis and the ionic strength by the addition of a salt, for example sodium chloride, ammonium sulfate, sodium sulfate, sodium, ammonium, or potassium phosphate, acetate, carbonate, citrate, or the like. Phosphates, carbonates, or citrates are particularly suitable salts because they have a buffer action and thus control both the ionic strength and the hydrogen ion concentration. For the precipitation of fibrinogen the pH may initially be adjusted in the neighborhood of 6.0 to 7.8. An ionic strength of 0.05 is adequate for effecting electrical discharge and flocculation; higher ionic strengths (e. g. 0.15 or more) are sometimes desirable for buffering.

The moist precipitate thus secured contains approximately 20 per cent protein of which 45 to 65 per cent is fibrinogen.

While it is possible to dissolve the moist precipitate in a solution of sodium citrate and then to freeze and dry from the frozen state to produce a stable powder which can be stored and afterwards redissolved, for the purposes of this invention a fibrinogen solution may be prepared directly from the moist precipitate and immediately processed into foams of this invention. For this purpose the moist precipitate is taken up in a citrate buffer of pH 6.05±0.05 and ionic